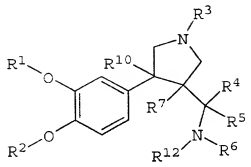
WHAT IS CLAIMED IS:

1. A compound having the formula:



wherein R^1 is lower alkyl, bridged alkyl, aryl, heteroaryl, aralkyl, cycloalkyl, a 5- or 6-membered saturated heterocycle, C_{1-4}alkylenearyl, C_{1-4}alkyleneOaryl, C_{1-4}alkyleneheteroaryl, C_{1-4}alkylene-Het, C_{2-4}alkylenearylOaryl, C_{1-4}alkylene bridged alkyl, C_{1-3}alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, or halocycloalkyl;

R^2 is hydrogen, methyl, or halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, lower alkyl, bridged alkyl, cycloalkyl, haloalkyl, halocycloalkyl, C_{1-3}alkylenecycloalkyl, a 5- or 6-membered saturated heterocycle, aryl, heteroaryl, C_{1-3}alkyleneC(=O)R^7, $C(=O)C(=O)NR^8R^9$, C_{1-4}alkyleneOR^7, C_{1-3}alkylenearyl, SO_2heteroaryl, Het, aralkyl, alkaryl, heteroaralkyl, heteroalkaryl, C_{1-3}alkyleneC(=O)OR^7, $C(=O)C_{1-3}$alkyleneC(=O)OR^7, C_{1-3}alkyleneheteroaryl, $C(=O)C(=O)OR^7$, $C(=O)C_{1-3}$alkyleneC(=O)OR^7, C(=O)-

C_{1-3}alkyleneNH(C=O)OR^7, C(=O)C alkyleneNH$_2$, and NHC(=O)OR^7;

R^4 is hydrogen, lower alkyl, haloalkyl, cycloalkyl, or aryl;

R^5 is hydrogen, lower alkyl, alkynyl, haloalkyl, cycloalkyl, or aryl;

R^6 and R^{12}, independently, are hydrogen, lower alkyl, aralkyl, SO_2R^{11}, or $C(=O)R^7$;

R^7 is selected from the group consisting of branched or unbranched lower alkyl, heteroaryl, a heterocycle, aralkyl, and aryl, and R^7 can be optionally substituted with one or more of RO^8, NR^8R^9, or SR^8;

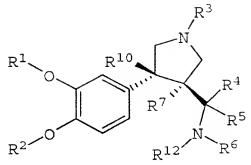
R^8 and R^9, same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, alkaryl, heteroaralkyl, heteroalkaryl, and aralkyl, or R^8 and R^9 can be taken together form a 4-membered to 7-membered ring;

R^{10} is hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, C(=O)alkyl, C(=O)cycloalkyl, C(=O)aryl, C(=O)Oalkyl, C(=O)Ocycloalkyl, C(=O)aryl, CH_2OH, CH_2Oalkyl, CHO, CN, NO_2, or SO_2R^{11};

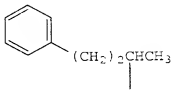
R^{11} is alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, or NR^8R^9;

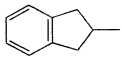
salts and solvates thereof.

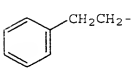
2. The compound of claim 1 having the structure:



3. The compound of claim 1 wherein R^2 is selected from the group consisting of:







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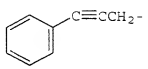

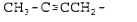

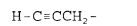

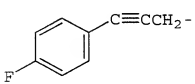

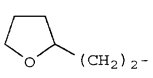

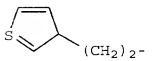

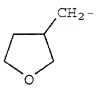

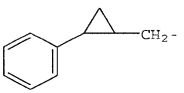

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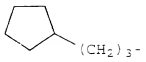

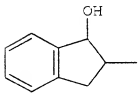

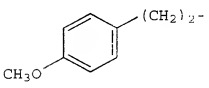

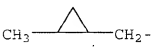

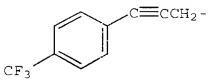

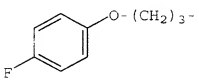

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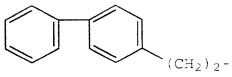
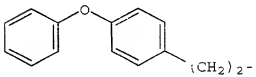
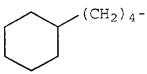
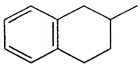
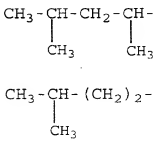








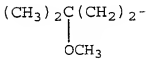


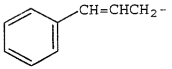
H-

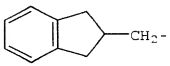
CH_3-

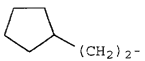
$(CH_3)_3C$-

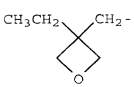
$(CH_3)_3C(CH_2)_2$

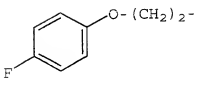


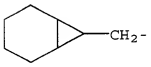


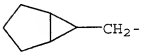


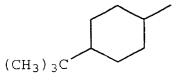


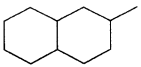


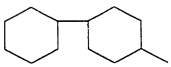


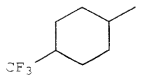


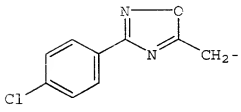


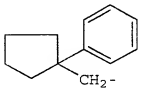


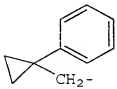


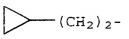


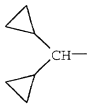












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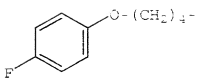

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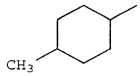
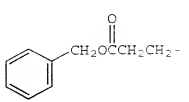
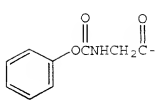
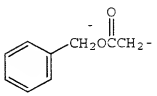
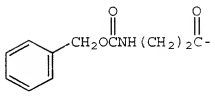


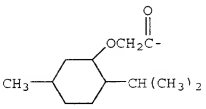
4. The composition of claim 1 wherein R^1 is selected from the group consisting of:

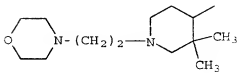


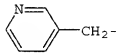


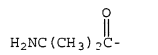


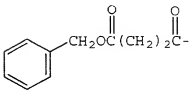


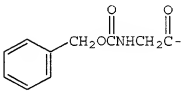


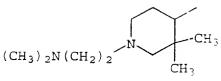


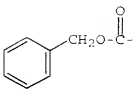


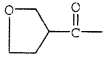


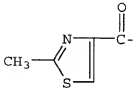


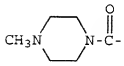


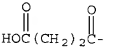


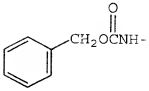


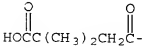


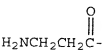


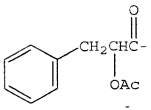


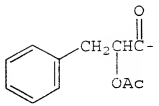


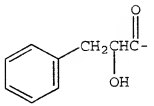


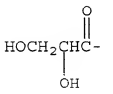


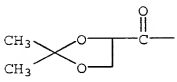


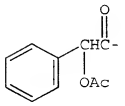


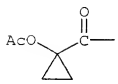


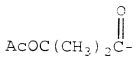












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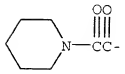

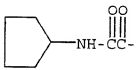

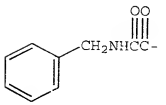

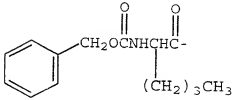

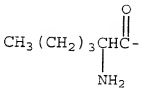

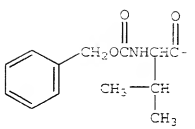

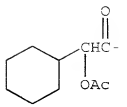

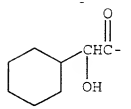

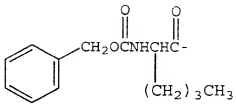

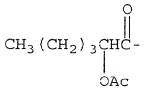

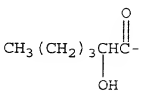

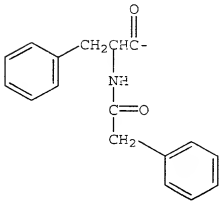

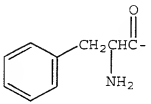

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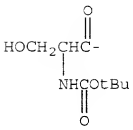

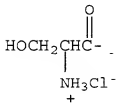

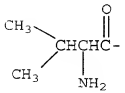

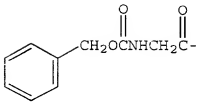

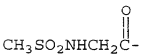

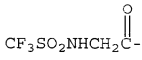

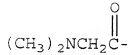

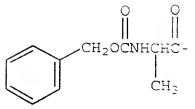

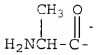

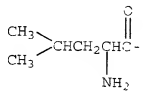

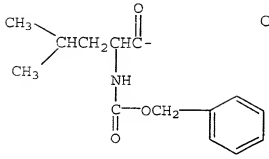

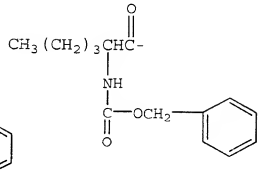

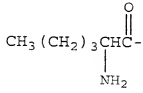

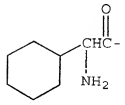

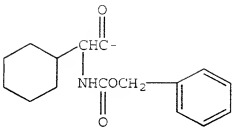

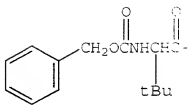

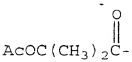

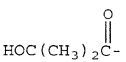

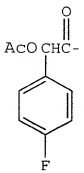

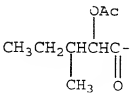

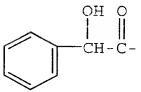

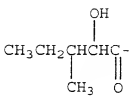

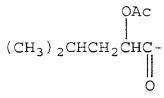

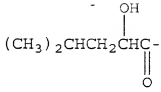

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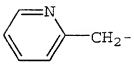


5. The compound of claim 1 wherein R^1 is selected from the group consisting of hydrogen, methyl, trifluoromethyl, cyclopropyl, ethynyl, and phenyl.

6. The compound of claim 1 wherein R^2 is hydrogen or lower alkyl.

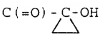
7. The compound of claim 1 wherein R^3 is selected from the group consisting of hydrogen, $C(=O)R^7$, $C(=O)OR^7$, ethyl, benzyl, SO_2CH_3, and $SO_2C_6H_5$.

8. The compound of claim 1 wherein R^7 is lower alkyl.

9. The compound of claim 1 wherein R^8 and R^9, independently, are hydrogen or lower alkyl, or are taken together form a 5-membered or 6-membered ring.

10. The compound of claim 1 wherein R^{12} is selected from the group consisting of hydrogen and lower alkyl.

11. The compound of claim 1 wherein R^1 is selected from the group consisting of cyclopentyl, cyclopropylmethyl, tetrahydrofuryl, indanyl, norbornyl, phenethyl, and phenylbutyl; R^2 is selected from the group consisting of methyl and difluoromethyl; R^3 is selected from the group consisting of benzyl, CO_2CH_3, $C(=O)CH_2OH$, $C(=O)CH(CH_3)OH$, $C(=O)C(CH_3)_2OH$, and



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R^4 is hydrogen; R^5 is hydrogen or methyl; R^6 is selected from the group consisting of hydrogen, methyl, ethyl, benzoyl, SO_2CH_3, $SO_2C_6H_5$, benzyl, $C(=O)C(CH_3)_3$, and acetyl; R^{17} is hydrogen or methyl; R^7 is methyl; and R^{12} is hydrogen.

12. The compound of claim 1 selected from the group consisting of

Methyl (4S,3R)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-3-{[benzylamino]methyl]}pyrrolidine carboxylate

Methyl (4S,3R)-3-(aminomethyl)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methylpyrrolidinecarboxylate

Methyl (3S,4S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-3-{[methylsulfonyl)amino]methyo}pyrrolidinecarboxylate

Methyl (4S,3R)-3-[(acetylamino)methyl]-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methylpyrrolidine-carboxylate

Methyl (4S,3R)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-3-[(phenylcarbonylamino)methyl]pyrrolidinecarboxylate

Methyl (3S,4S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-3-{[phenylsulfonyl)amino]methyl}pyrrolidinecarboxylate

Bis{[(4S,3R)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-carboxymethylpyrrolidin-3-yl]methyl}amine

1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethylamine

1-{(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethylamine

N-{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}benzamide

N-{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}benzamide

N-{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}acetamide

N-{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}acetamide

3-(S)-(1-Acetylaminoethyl)-4-(S)-(3-cyclopentyloxy-4-methoxyphenyl)-3-methylpyrrolidine-1-carboxylic acid methyl ester

{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}-(phenylsulfonyl)amine

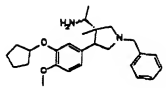
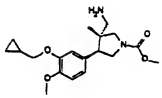
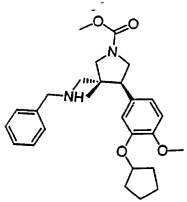
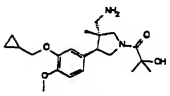
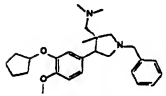
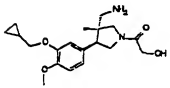
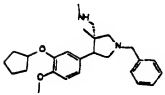
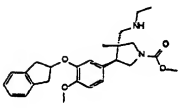
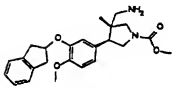
{1-[(3S,4S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}-(phenylsufonyl)amine

{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}-(methylsulfonyl)amine

{1-[(3S,4S)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-3-methyl-1-benzylpyrrolidin-3-yl]ethyl}-(methylsulfonyl)amine, and

Methyl (3S,4S)-4-(3-cyclopentyloxy-4-methoxyphenyl)-3-methyl-3-[(methylamino)ethylpyrrolidine carboxylate.

13. The compound of claim 1 selected from the group consisting of

14. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 1 nM to about 25 μM.

15. The compound of claim 1 having a PBL/TNFα EC_{50} of about 10 nM to about 20 μM.

16. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 1 nM to about 25 μM, and a PBL/TNFα EC_{50} of about 10 nM to about 25 μM.

17. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 100 x 10^{-6} M or less.

18. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 50 x 10^{-6} M or less.

19. The compound of claim 1 having a PBL/TNFα EC_{50} of about 5 μM or less.

20. The compound of claim 1 having a PBL/TNFα EC_{50} of about 2 μM or less.

21. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 100 x 10^{-6} or less and a PBL/TNFα EC_{50} of about 5 μM or less.

22. The compound of claim 1 having an IC_{50} vs. human recombinant PDE4 of about 50 x 10^{-6} or less and a PBL/TNFα EC_{50} of about 2 μM or less.

23. A pharmaceutical composition comprising a compound of claim 1, a pharmaceutically acceptable carrier, and, optionally, a second antiinflammatory therapeutic agent.

24. The composition of claim 23 wherein the second antiinflammatory therapeutic agent is capable of targeting TNFα.

25. A method of treating a mammal having a condition where inhibition of a cAMP-specific PDE is of therapeutic benefit, said method comprising administering to said mammal at therapeutically effective amount of a compound of claim 1.

26. A method of modulating cAMP levels in a mammal comprising administering to said mammal an effective amount of a compound of claim 1.

27. A method of treating a mammal having a condition where inhibition of a cAMP-specific PDE is of a therapeutic benefit comprising administering to said mammal an effective amount of a pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

28. The method of claim 27 wherein the condition is an allergic disease, an autoimmune disease, an inflammatory disease, an arthritic disease, or dermititis.

29. The method of claim 27 wherein the condition is rheumatoid arthritis, osteoarthritis, gouty arthritis, or spondylitis.

30. The method of claim 27 wherein the condition is thyroid-associated ophthalmopathy, Behcet disease, sepsis, septic shock, endotoxic shock, gram negative sepsis, gram positive sepsis, toxic shock syndrome, allergic conjunctivitis, vernal conjunctivitis, or eosinophilic granuloma.

31. The method of claim 27 wherein the condition is asthma, chronic bronchitis, allergic rhinitis, adult respiratory distress syndrome, chronic pulmonary inflammatory disease, chronic obstructive pulmonary disease, silicosis, or pulmonary sarcoidosis.

32. The method of claim 27 wherein the condition is reperfusion injury of the myocardium, brain or extremities as a brain or spinal cord injury due to trauma.

33. The method of claim 27 wherein the condition is a fibrosis, keloid formation, or scar tissue formation.

34. The method of claim 27 wherein the condition is systemic lupus erythematosus, a transplant rejection disorder, a graft vs. host reaction, or an allograft rejection.

35. The method of claim 27 wherein the condition is chronic glomerulonephritis, an inflammatory bowel disease, Crohn's disease, or ulcerative colitis.

36. The method of claim 27 wherein the condition is proliferative lymphocytic disease or a leukemia.

37. The method of claim 27 wherein the condition is an inflammatory dermatosis, atopic dermatitis, psoriasis, or urticaria.

38. The method of claim 27 wherein the condition is a cardiomyopathy, congestive heart failure, atherosclerosis, pyrexia, cachexia, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome, ARC, cerebral malaria, osteoporosis, a bone resorption disease, fever and myalgias due to infection, erectile dysfunction, diabetes insipidus, a central nervous system disorder, depression, multi-infarct dementia, an anxiety or stress response, cerebral ischemia, tardive dyskinesia, Parkinson's disease, or premenstrual syndrome.

39. The method of claim 27 wherein the mammal exhibits a minimal emetic response.

40. The method of claim 27 wherein the mammal is free of an emetic response.

41. The method of claim 27 wherein the mammal exhibits minimal adverse central nervous system side effects.

42. The method of claim 27 wherein the mammal is free of adverse central nervous system side effects.

43. The method of reducing TNF levels in a mammal comprising administering to said mammal therapeutically effective amount of a compound of claim 1.

44. A method of suppressing inflammatory cell activation in a mammal comprising administering to said mammal a therapeutically effective amount of a compound of claim 1.

45. A method of inhibiting PDE4 function in a mammal comprising administering to said mammal a therapeutically effective amount of a compound of claim 1.